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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KOSSON, ROSANNE	

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,088	LEWIS ET AL.	
	Examiner	Art Unit	
	Rosanne Kosson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28,31,33-35 and 37-59* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,6,12,13,22-24,27,28,38-41,43,45,47,49 and 54-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 2-4,7-11,14-21,25,26,31,33-35,37,42,44,46,48 and 50-53.

DETAILED ACTION

The amendment filed on December 27, 2007 has been received and entered. Claims 1, 5, 6, 27 and 28 have been amended. No claims have been canceled. Claims 53-59 have been added.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

As discussed in the previous Office action, Applicants have elected Group 208, claims 1, 5, 6, 12-13, 22, 23, 27, 28, 38-41, 43, 45, 47 and 49, to the extent that these claims read on SEQ ID NO:5 or SEQ ID NO:3 in which Xaa5 and Xaa6 are both present and are any amino acid but C. New claims 53-59 will be examined to the extent that they read on the elected invention. But, the amended claims and the new claims read on a very large number of polypeptides that do not read on the elected on the elected invention. For example, the amended claims have been broadened to recite, and the new claims recite, genera of named substitution variants that do not read on SEQ ID NOS:3 and 5. The new claims also recite that Xaa5 and Xaa6 may be deleted, polypeptides that read on non-elected inventions. As previously discussed, the claims will be examined to the extent that they read on the elected invention only and are otherwise withdrawn. The restriction requirement and its finality have not changed. Accordingly, claims 1, 5, 6, 12-13, 22-24, 27, 28, 38-41, 43, 45, 47, 49 and 54-59 are examined on the merits herewith to the extent that they read on the elected invention. Claim 53 does not read on the elected invention, nor do portions of claim 55-57- substitutions of definite amino acids with different amino acids and polypeptides in which Xaa5 and Xaa6 are deleted.

To reiterate, the elected polypeptide sequences are EGVCCGYKLCXXC in which X is not C (the extent to which SEQ ID NO:5 reads on the elected sequence) and CCGYKLCXXC in which X is not C (the extent to which SEQ ID NO:3 reads on the elected sequence).

Regarding claim 24, because this claim depends from claim 1 and claim 5, it will be rejoined and examined to the extent that it reads on the elected invention (a polypeptide of 11-20 amino acids that comprises SEQ ID NO:3 or 5).

Claim Objections

In view of Applicants' amendments to the claims, the objections are withdrawn. Examiner had interpreted the slash ("/") in the claims to mean "also known as," i.e., that Applicants' meaning was that the neuronal amine transporter is also known as a noradrenaline transporter. But, Applicants' amendments to the claims have clarified that these are two different transporters or sets of transporters.

In claim 6, the word "said chain" in the penultimate line on p. 4 of the claims should be corrected to "side chain." This error appears to be a typographical error.

Claim 24 has been amended to depend from claim 1 or claim 5. SEQ ID NO:3 has 10 amino acids, and SEQ ID NO:5 has 13 amino acids. Thus, the claim should be amended to recite a polypeptide of claim 1 consisting of 11 to 20 amino acids or a polypeptide of claim 5 consisting of 13 to 20 amino acids. A polypeptide of claim 5 cannot consist of 11 or 12 amino acids. Fragments of SEQ ID NO:5 have not been claimed in any claim, and a polypeptide of 11 or 12 amino acids is not a polypeptide of SEQ ID NO:5. Appropriate correction is required.

Claim 27 is not a proper dependent claim, as it merely recites inherent properties of SEQ ID NO:3 and does not further limit claim 1, from which it depends. The inherent properties recited in this claim may be added to claim 1, or the claim may be canceled. Claim 27 may not

be written as an independent claim, because it would then be a duplicate of claim 1, as the two claims would be of the same scope.

Claim Rejections - 35 USC § 112, first paragraph

Claims 1, 5, 6, 12-13, 22, 23, 27, 28, 38-41, 43, 45, 47 and 49 are again rejected, and claims 24 and 54-59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection was discussed in the previous Office action.

Applicants' amendments to the claims recite specific amino acids and amino acid derivatives that are used to make variant polypeptides, rather than any amino acid. But, as discussed above, the claims now read on many non-elected polypeptide sequences. Additionally, although the type or types of transport proteins that are inhibited by SEQ ID NO:3 and 5 are activities that are inherent properties of these polypeptides, as noted above, the claim amendments specify that a neuronal amine transporter is different from a noradrenaline transporter, because one of the types has been deleted. The specification also makes it clear that these are two different transporters (or groups of transporters), because SEQ ID NOS:3 and 5 inhibit the noradrenaline transporter or noradrenaline transporters, but not serotonin reuptake transporters or adrenoceptors, i.e., other amine-containing neurotransmitter transporter proteins (see pp. 9-10). Serotonin and adrenaline are also amine-containing neurotransmitters. To delete the claim portions reciting non-elected inventions, and to correct the description of the transporter proteins that are inhibited, the claims may be amended as follows, using the following claims as models for the remaining claims.

1. (currently amended) An isolated, synthetic or recombinant χ-conotoxin peptide having the ability to inhibit ~~neuronal amine~~ a noradrenaline transporter comprising the following sequence of amino acids:
Cys Cys Gly Tyr Lys Leu Cys Xaa5 Xaa6 Cys (SEQ ID NO. 3)
where Xaa5 and Xaa6 ~~are independently absent or~~ represent any amino acid residue except Cys; or a sequence in which Gly, Tyr, Lys or Leu are subject to ~~conservative amino acid substitution or side~~ chain modification, wherein said ~~substitution or~~ side chain modification for Tyr is a substitution of Tyr with MeY, ~~Phe or Trp,~~ and said ~~substitution or~~ side chain modification for Leu is a substitution of Leu with ~~Val, Ile,~~ Hle or Nle; with the proviso that the peptide is not χ-MrIA, χ-MrIB, Mar2, CMrVIA, Bn1.5, Mr1.3 or Au1.4; or a salt, ester, amide, prodrug or cyclised derivative thereof.

5. (currently amended) The χ-conotoxin peptide according to claim 1 comprising the following sequence of amino acids:
Xaa1 Xaa2 Xaa3 Xaa4 Cys Cys Gly Tyr Lys Leu Cys Xaa5 Xaa6 Cys (SEQ ID NO:5)
where Xaa1 is an N-terminal residue and is ~~selected from~~ either pGlu[[,]] or DpGlu, ~~Pro, Hyp or an N-acetylated amino acid residue;~~
Xaa2 is ~~selected from Arg, Asn, Lys, BHK, Orc, Lys, DArg, Nle, DLys, DMK, DAsn, Thr, ABZ, Nap, Cit, Val and~~ a deletion,
Xaa3 is ~~selected from~~ Gly, ~~Asp, Lys, Arg, Ala, Nle and Ser,~~
Xaa4 is ~~selected from~~ Val, ~~Leu, Nle, Ile, Thr, Ala and Abu,~~ and
Xaa5 and Xaa6 ~~are independently absent or~~ represent any amino acid residue except Cys; or such a sequence where one or more of the [[loop 1]] residues Gly, Tyr, Lys and Leu are subject to ~~conservative amino substitution or sidechain~~ side-chain modification, wherein said ~~substitution or~~ side chain modification for Tyr is a substitution of Tyr with MeY, ~~Phe or Trp,~~ and said ~~substitution or~~ side chain modification for Leu is a substitution of Leu with ~~Val, Ile,~~ Hle or Nle, or a salt, ester, amide, prodrug or cyclised derivative thereof.

6. (currently amended) The χ-conotoxin peptide according to claim 5 consisting of the following sequence of amino acids:
Xaa1 Xaa2 Xaa3 Xaa4 Cys Cys Gly Tyr Lys Leu Cys Xaa5 Xaa6 Cys (SEQ ID NO:5)

where Xaa1 is an N-terminal residue and is ~~selected from~~ either pGlu[[,]] or DpGlu, ~~Pro, Hyp or an N-acetylated amino acid residue;~~
Xaa2 is ~~selected from Arg, Asn, Lys, BHK, Orc, Lys, DArg, Nle, DLys, DMK, DAsn, Thr, ABZ, Nap, Cit, Val and~~ a deletion,
Xaa3 is ~~selected from~~ Gly, ~~Asp, Lys, Arg, Ala, Nle and Ser,~~
Xaa4 is ~~selected from~~ Val, ~~Leu, Nle, Ile, Thr, Ala and Abu,~~ and
Xaa5 and Xaa6 ~~are independently absent or~~ represent any amino acid residue except Cys; or such a sequence where one or more of the [[loop 1]] residues Gly, Tyr, Lys and Leu are subject to ~~conservative amino substitution or sidechain~~ side-chain modification, wherein said ~~substitution or~~ side chain modification for Tyr is a substitution of Tyr with MeY, ~~Phe or Trp,~~ and said ~~substitution or~~ side chain modification for Leu is a substitution of Leu with ~~Val, Ile,~~ Hle or Nle, or a salt, ester, amide, prodrug or cyclised derivative thereof.

43. (currently amended) The peptide according to claim 5, wherein Xaa5 is selected from the group consisting of His, Arg, Trp, Nal, and Glu ~~and a deletion~~.

47. (currently amended) The peptide according to claim 5, wherein Xaa6 is selected from the group consisting of Hyp, Pro, Ala, Tic, Pip, MeY, DMD, Phe, THZ, Glu, Nle, and Tyr ~~and a deletion~~.

Regarding the enablement rejection, in view of Applicants' amendments to the claims, this rejection is withdrawn.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5, 6 and 59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 59 recites indefinite language with respect to the

disulfide bonds, rendering the meaning of the claims unclear. The claim may be amended as follows:

The peptide according to claim 1, 5 or 6, wherein the peptide has one disulfide bond between the cysteines at amino acid positions 1 and 10 in SEQ ID NO:3 or between the cysteines at amino acid positions 4 and 13 in SEQ ID NO:5 and a second disulfide bond between the cysteines at amino acid positions 2 and 7 in SEQ ID NO:3 or between the cysteines at amino acid positions 5 and 10 in SEQ ID NO:5.

Claims 5, 6, 12-13, 22-24, 27, 28, 38-41, 43, 45, 47, 49 and 54-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims, which depend from claim 1, recite the term "loop 1" residues or various amino acid in "loop 1." Claim 1 does not recite "loop 1." Thus, there is insufficient antecedent basis for this limitation in the claims. Appropriate correction is required. The term may be deleted.

Claim Rejections - 35 USC § 102

Claims 1, 27 and 28 are again rejected, and claims 24 and 59 are rejected, under 35 U.S.C. 102(e) as being anticipated by McIntosh et al. (US 6,767,896 B1). This rejection was discussed in the previous Office action. McIntosh et al. disclose compositions comprising the conotoxin polypeptides Mar1 (SEQ ID NO:12) and Q818 (SEQ ID NO:14), which comprise the sequence of Applicants' SEQ ID NO:3- CCGYKLCXXC (see col. 6, lines 57-62; col. 10, line 66, to col. 15, line 54; col. 20, Table 1; and col. 22, Table 2). McIntosh et al. also disclose the polypeptide of their SEQ ID NO:3, which is a polypeptide of 12 amino acids that comprises instant SEQ ID NO:3 (see col. 4, lines 1-42).

Additionally, McIntosh et al. disclose that the disulfide binding in the polypeptide

sequence corresponding to instantly claimed SEQ ID NO:3 is C1 – C4 and C2 – C3 (see col. 22, lines 5-10).

Applicants assert that McIntosh et al. disclose larger polypeptides of which SEQ ID NO:3 is a fragment and that therefore, these polypeptides are not χ-conotoxins. Applicants assert that the disulfide bonding of a χ-conotoxin is as recited in claim 59.

In reply, Applicants have not amended the comprising language of these claims, and the prior art discloses polypeptides comprising the claimed polypeptide, SEQ ID NO:3. Applicants have not claimed the truncation fragment or mature form of SEQ ID NO:3. Although the precursor forms are longer than the mature polypeptides, McIntosh et al. do disclose the mature form of several of their conotoxins, and these mature forms are naturally occurring short forms 11-13 amino acids in length that are analgesics, SEQ ID NOS:2 – 7 (see col. 1, lines 2-8; and col. 4, lines 1-55). In particular, the Mar2 polypeptide, SEQ ID NO:3 in which Xaa1 is Y, Xaa2 is K and Xaa3 is hydroxy-P, is a fragment of Applicants' SEQ ID NO:5 and is instantly claimed SEQ ID NO:5 minus the N-terminal E. Mar1 of McIntosh et al. is a version of their SEQ ID NO:2 in which Xaa1 is Y, Xaa2 is K and Xaa3 is hydroxy-P. Instantly claimed SEQ ID NO:5 differs from Mar1 in that the N-terminal amino acid is E, vs. the N of Mar1.

As for disulfide bonding, claims 1, 27 and 28 do not recite that SEQ ID NO:3 has a disulfide bond between any two C residues. The claims do not recite an upper limit for the length of the polypeptides. Thus, the claim language implies that it is the presence of SEQ ID NO:3 or 5 that confers the particular activity, not the length of the polypeptide. The disulfide bonds may form spontaneously in vivo or in vitro, as disulfide bonding in a three-dimensional structure is determined by the amino acid sequence. As noted above, McIntosh et al. disclose that the disulfide bonds in their short Mar peptides have the arrangement of C1 – C4 and C2 – C3.

In view of the foregoing, the rejection of record is maintained.

Claims 1, 27 and 28 are again rejected, and claim 24 is rejected, under 35 U.S.C. 102(e) as being anticipated by Olivera et al. (US 2003/0109670 A1). This rejection was discussed in the previous Office action. Olivera et al. disclose a composition comprising the conotoxin polypeptide Mr1.1 (SEQ ID NO:352), which comprises the sequence of Applicants' SEQ ID NO:3- CCGYKLCXXC (see p. 41, Table 5; and paragraphs 3, 5, 6, 9, 11, 23, 24 and 48-56). Olivera et al. also disclose SEQ ID NO:353, a toxin polypeptide of 12 amino acids that comprises the polypeptide of instant SEQ ID NO:3 (see pp. 33, 147 and 148).

Similarly to the above rejection, Applicants assert that Olivera et al. disclose a larger polypeptide of which SEQ ID NO:3 is a fragment and that, therefore, this polypeptide is not a χ-conotoxin.

In reply, as discussed above, Applicants have not amended the comprising language of these claims, and the prior art discloses a polypeptide comprising the claimed polypeptide, SEQ ID NO:3. Applicants may claim the truncation fragment of SEQ ID NO:3. As previously discussed, Olivera et al. do disclose that their polypeptide is an inhibitor of neurotransmitter activity, and many neurotransmitters contain amine groups and have transporter proteins. Applicants discuss above that a feature of χ-conotoxins is their pattern of disulfide bonds, bonds between the C's at amino acid positions 1 and 10 and 2 and 7, in the case of SEQ ID NO:3. But, as discussed above, claims 1, 27 and 28 do not recite that SEQ ID NO:3 has a disulfide bond between any two C residues.

In view of the foregoing, the rejection of record is maintained.

Double Patenting- Obviousness-type

Claims 1, 5, 6, 12-13, 22, 23, 27, 28, 38-41, 43, 45, 47 and 49 are again provisionally rejected, and claims 54-59 are rejected, on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of copending Application No. 10/537,704. Although the conflicting claims are not identical, they are not patentably distinct from each other because each set of claims is drawn to a composition comprising the same polypeptide, instantly claimed SEQ ID NO:5. Each set of claims recites the same invention with slightly different wording that amounts to a semantic equivalent. Thus, the two inventions are not patentably distinct. This rejection was discussed in the previous Office action.

Applicants have declined to respond to the rejection at this time. Accordingly, the rejection is maintained and is still outstanding.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosanne Kosson whose telephone number is 571-272-2923. The examiner can normally be reached on Monday-Friday, 8:30-6:00, alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private

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Rosanne Kosson
Examiner, Art Unit 1652

rk/2008-01-15

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PRIMARY EXAMINER